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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/595,720	06/16/2000	John C. Cheronis	233/111	1455

2101 7590 05/21/2002

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EXAMINER
COOK, LISA V

ART UNIT	PAPER NUMBER
1641	10

DATE MAILED: 05/21/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/595,720	Applicant(s) CHERONIS ET AL.	
	Examiner Lisa V. Cook	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *29-32 and 34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28 and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-34* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 June 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicants' election of Group I – claims 1-28 and 33 with out traverse is acknowledged. (See paper#8, filed 1/24/02).

2. Currently, claims 1-28 and 33 are currently pending and under examination.

Information Disclosure Statement

3. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the Examiner on form PTO-892 or Applicant on form PTO-1449 has cited the references they have not been considered. (For example, see listing of references).

4. The IDS filed on 7/26/00, Paper#4 has been considered as to the merits prior to first action.

Drawings

5. This application has been filed with informal drawings, which are acceptable for examination purposes only. New formal drawings are required in this application. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Specification

6. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

7. Claims 1-28 and 33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 1, step (d) is vague and indefinite in reciting the recovery of a second sample because it is not clear if the second sample is recovered from step (c) or will another totally independent sample be analyzed in the assay procedure? In other words, it is not clear if Applicant intends to mean the first sample (aptamer bound target molecules) of step (c) will be further analyzed or is a second sample independent of the first sample being processed? Please clarify.

B. Claim 1 is vague and indefinite because a detection step is not recited in the method. As supported by Applicant, quantification is usually accomplished by detection of a fluorescent or radioactive moiety incorporated in the formed complex (page 1, lines 18-20). A detection step should be added. Appropriate correction required.

C. The term "substantially all" in claim 1 is a relative term which renders the claim indefinite. The term " substantially all " is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree (not listed on page 10-11), and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear what is intended to be substantially all, will all the molecules bind or not? How will the total binding of all the molecules be assessed (known amounts utilized)? The term should be removed from the claim.

D. Claims 3 and 4 are vague and indefinite in utilizing the phrase " molar concentrations less than/equal to/or greater than their dissociation constants with respect to the aptamers. It is not clear

E. Regarding claims 15, 17, and 18, the phrase "including " renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

F. "The sample" in claims 14 and 15 lack antecedent basis. It is suggested the claims read "first sample" or "second sample" in order to obviate this rejection.

G. Claim 15 is in improper Markush form, because and was omitted from the listed samples. It is suggested that "and" be incorporated in to the claim after "vascular tissue".

8. Claims 1-28 and 33 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are explained below:

The claims are drawn to assay techniques that measure complex formation and separation. However, the instant claims do not indicate how the complex will be identified (i.e. label). An assay, as recited in the preamble of claims 1 requires at least a contact step between reagents and sample, a detection step, and a correlation step. Please include the appropriate assay steps.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-28 and 33 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure, which is not enabling. The methods/substances of independent claim 1 have insufficient steps. These critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). Merely, reciting the use of reagents in an assay format is not considered a proper method step. An assay as recited in the preambles of claim 1 requires at least a contact step between reagent and sample – resulting in binding/complex formation, separation, detection, and a correlation step directed to the analysis of interest. The recited claims do not include the required steps for detection. Please add the label to the claims.

Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 6, 7, 15, and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Griffin et al. (US 5,756,291).

Griffin et al. disclose a method of detecting thrombin using a labeled DNA aptamers (nucleic acid aptamer), which specifically bind thrombin (target molecule). The method measures complexes formed when the target molecule is reacted with a mixture of oligonucleotides containing random sequences and sequences that serve as primer for PCR-polymerase chain reaction (the first sample). A complex is formed with the specific binding sequences but not with the other members of the oligonucleotide mixture.

The complex is the separated from uncomplexed oligonucleotides (second sample) and sequenced via successive rounds of selection employing complexation, separation, amplification, and recovery. The target molecules including serum (blood) proteins, kininins, eicosanoids and extracellular proteins. See abstract. The aptamers may be bound to solid phase/supports and employed to separate target molecules form contaminants (unbound materials) in a sample. See column 12, line 63 through column 13, line 8.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

I. Claims 3, 4, 5, 8-14, 18, and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Griffin et al. (US Patent #5,756,291) in view of Schultz et al. (US Patent #6,180,415).

See Griffin et al. as set forth above.

Griffin et al. differ from the instant invention in not specifically teaching target molecules that are low abundance molecules present in that sample at various dissociations constants (while monitoring the presence of the aptamer) employing support matrixes including beads (particles).

However, Schultz et al. disclose plasmon resonant particle (PRP) method and apparatus for measuring a target molecule in a sample. The method involves the detection of an analyte present in a sample (presence/amount). Abstract A ligand is bound to the particles and may be one of a conjugate pair, such as antigen/antibody, hormone/receptor, drug/receptor, effectors/receptor, enzyme/substrate, lipid/lipid binding agent, and complementary nucleic acid strands. Column 5 lines 16-29 and column 8 line 65 through column 9 line 5.

The PRP can be associated with tissue sections, cells, grids, and metals. Column 25 line 64 through column 26 line 26. The methods that employ the inventive new types of probes can bind selected conjugates to the PRP therein detecting low abundance molecules. Column 31, lines 23-33.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to detect low abundance molecules with respect to the concentration of the aptamer in particle configurations (beads) as taught by Schultz et al. in the method of Griffin to detect bio-molecules because Schultz et al. taught that the predefined mixtures of PRP [incorporating the ligand] are especially useful in improving the accuracy of detection of low abundance molecules. Column 31, lines 23-33.

II. Claims 16-17, 24-28 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Griffin et al. (US Patent #5,756,291) in view of Schultz et al. (US Patent #6,180,415) in further view of Wiegand et al. (WO 96/10576).

See Griffin et al. in view of Schultz et al. as set forth above.

Griffin et al. in view of Schultz et al. differ from the instant invention in not disclosing environmental sampling, target molecules including IgE, antibody binding characteristics, and ligands having the apatmer-binding characteristics.

Wiegand et al. disclose these limitations in their method. Oligonucleotide ligands to immunoglobulin IgE are formed and utilized. See page 1. The method is taught to be useful in IgE dependent reactions, which cause allergic disease.

The procedure can be used to detect common allergens such as pollen, dust mites, certain food, animal dander, fungal spores, and insect venoms. Page 2, lines 5-6. The method includes nucleic acid ligands that have substantially the same ability to bind IgE as the nucleic ligands (apatmer) used in the assay procedure (Tables 1, 5, and 6 – Page 15, lines 25-31).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to detect IgE target molecules as taught by Wiegand et al. in the method of Griffin et al. in view of Schultz et al. because of IgE's importance in allergic response. Since approximately 20% of the US population is prone to developing an abnormally strong immediate hypersensitivity –allergy, its detection is essential to evaluation and cures. Page 1 line 20 through page 2 line 6. A person of ordinary skill in the art would have had a reasonable expectation of success utilizing and detecting IgE, because Wiegand et al. shown DNA ligands that were operable in this process with high affinity and accuracy. Page 38, lines 3-12.

With respect to the antibody binding characteristics recited in claims 26-28 these limitations are view as inherent properties, which are found in all antibodies. Absent evidence to the contrary they are viewed as obvious limitations found in antibodies.

A claim is anticipated if each element of the claim is found, either expressly described or under principles of inherency, in a single prior art reference, or that the claimed invention was previously known or embodied in a single prior art device or practice.

It has been held that the recitation that an element is "capable of" performing a function is not a positive limitation but only requires the ability to so perform. It does not constitute a limitation in any patentable sense. *In re Hutchison*, 69 USPQ 138.

III. Claims 19, 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Griffin et al. (US Patent #5,756,291) in view of Schultz et al. (US Patent #6,180,415) in further view of Sampson et al. (US Patent #6,054,274).

See Griffin et al. in view of Schultz et al. as set forth above.

Griffin et al. in view of Schultz et al. differ from the instant invention in not disclosing ligand immobilization on an affinity column or denaturing procedures in their methods.

However, Sampson et al. disclose methods of amplifying target nucleic acid sequence analytes. The method includes repeating signal amplification sequencing (figure 1), denaturing (figure 3), and column separation techniques (polymerization and hybridization). See column 5, line 23 through column 6, line 33.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize denaturing procedures and/or column separation procedures such as hybridization/polymerization as taught by Sampson et al. in the method of Griffin et al. (US Patent #5,756,291) in view of Schultz et al. (US Patent #6,180,415) Griffin et al. taught that the inventive method allowed for multiple hybridization and polymerization to produce enhanced detection of a target nucleic acid sequence. Column 3, lines 24-50.

A person of ordinary skill in the art would have had a reasonable expectation of success utilizing such materials, because they were already shown to be operable in the prior art.

One having ordinary skill in the art would have been motivated to do this because of the increased flexibility in detecting and analyzing the target molecule.

12. For reasons aforementioned, no claims are allowed.

Remarks

13. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

Nazarenko et al. (US Paten #5,866,336) disclose methods involving oligonucleotides with molecular energy transfer labels.

14. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 308-4242, which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (703) 305-0808. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Lisa V. Cook
CM1-7B17
(703) 305-0808
5/20/02

DETAILED ACTION

Election/Restrictions

1. Applicants' election of Group I – claims 1-28 and 33 with out traverse is acknowledged. (See paper#8, filed 1/24/02).

2. Currently, claims 1-28 and 33 are currently pending and under examination.

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4. The IDS filed on 7/26/00, Paper#4 has been considered as to the merits prior to first action.

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B. Claim 1 is vague and indefinite because a detection step is not recited in the method. As supported by Applicant, quantification is usually accomplished by detection of a fluorescent or radioactive moiety incorporated in the formed complex (page 1, lines 18-20). A detection step should be added. Appropriate correction required.

C. The term "substantially all" in claim 1 is a relative term which renders the claim indefinite. The term " substantially all " is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree (not listed on page 10-11), and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear what is intended to be substantially all, will all the molecules bind or not? How will the total binding of all the molecules be assessed (known amounts utilized)? The term should be removed from the claim.

D. Claims 3 and 4 are vague and indefinite in utilizing the phrase " molar concentrations less than/equal to/or greater than their dissociation constants with respect to the aptamers. It is not clear

E. Regarding claims 15, 17, and 18, the phrase "including " renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

F. "The sample" in claims 14 and 15 lack antecedent basis. It is suggested the claims read "first sample" or "second sample" in order to obviate this rejection.

G. Claim 15 is in improper Markush form, because and was omitted from the listed samples. It is suggested that "and" be incorporated in to the claim after "vascular tissue".

8. Claims 1-28 and 33 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are explained below:

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9. Claims 1-28 and 33 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure, which is not enabling. The methods/substances of independent claim 1 have insufficient steps. These critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). Merely, reciting the use of reagents in an assay format is not considered a proper method step. An assay as recited in the preambles of claim 1 requires at least a contact step between reagent and sample – resulting in binding/complex formation, separation, detection, and a correlation step directed to the analysis of interest. The recited claims do not include the required steps for detection. Please add the label to the claims.

Rejections - 35 USC § 102

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A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 6, 7, 15, and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Griffin et al. (US 5,756,291).

Griffin et al. disclose a method of detecting thrombin using a labeled DNA aptamers (nucleic acid aptamer), which specifically bind thrombin (target molecule). The method measures complexes formed when the target molecule is reacted with a mixture of oligonucleotides containing random sequences and sequences that serve as primer for PCR-polymerase chain reaction (the first sample). A complex is formed with the specific binding sequences but not with the other members of the oligonucleotide mixture.

The complex is the separated from uncomplexed oligonucleotides (second sample) and sequenced via successive rounds of selection employing complexation, separation, amplification, and recovery. The target molecules including serum (blood) proteins, kininins, eicosanoids and extracellular proteins. See abstract. The aptamers may be bound to solid phase/supports and employed to separate target molecules form contaminants (unbound materials) in a sample. See column 12, line 63 through column 13, line 8.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

I. Claims 3, 4, 5, 8-14, 18, and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Griffin et al. (US Patent #5,756,291) in view of Schultz et al. (US Patent #6,180,415).

See Griffin et al. as set forth above.

Griffin et al. differ from the instant invention in not specifically teaching target molecules that are low abundance molecules present in that sample at various dissociations constants (while monitoring the presence of the aptamer) employing support matrixes including beads (particles).

However, Schultz et al. disclose plasmon resonant particle (PRP) method and apparatus for measuring a target molecule in a sample. The method involves the detection of an analyte present in a sample (presence/amount). Abstract A ligand is bound to the particles and may be one of a conjugate pair, such as antigen/antibody, hormone/receptor, drug/receptor, effectors/receptor, enzyme/substrate, lipid/lipid binding agent, and complementary nucleic acid strands. Column 5 lines 16-29 and column 8 line 65 through column 9 line 5.

The PRP can be associated with tissue sections, cells, grids, and metals. Column 25 line 64 through column 26 line 26. The methods that employ the inventive new types of probes can bind selected conjugates to the PRP therein detecting low abundance molecules. Column 31, lines 23-33.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to detect low abundance molecules with respect to the concentration of the aptamer in particle configurations (beads) as taught by Schultz et al. in the method of Griffin to detect bio-molecules because Schultz et al. taught that the predefined mixtures of PRP [incorporating the ligand] are especially useful in improving the accuracy of detection of low abundance molecules. Column 31, lines 23-33.

II. Claims 16-17, 24-28 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Griffin et al. (US Patent #5,756,291) in view of Schultz et al. (US Patent #6,180,415) in further view of Wiegand et al. (WO 96/10576).

See Griffin et al. in view of Schultz et al. as set forth above.

Griffin et al. in view of Schultz et al. differ from the instant invention in not disclosing environmental sampling, target molecules including IgE, antibody binding characteristics, and ligands having the apatmer-binding characteristics.

Wiegand et al. disclose these limitations in their method. Oligonucleotide ligands to immunoglobulin IgE are formed and utilized. See page 1. The method is taught to be useful in IgE dependent reactions, which cause allergic disease.

The procedure can be used to detect common allergens such as pollen, dust mites, certain food, animal dander, fungal spores, and insect venoms. Page 2, lines 5-6. The method includes nucleic acid ligands that have substantially the same ability to bind IgE as the nucleic ligands (apatmer) used in the assay procedure (Tables 1, 5, and 6 – Page 15, lines 25-31).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to detect IgE target molecules as taught by Wiegand et al. in the method of Griffin et al. in view of Schultz et al. because of IgE's importance in allergic response. Since approximately 20% of the US population is prone to developing an abnormally strong immediate hypersensitivity –allergy, its detection is essential to evaluation and cures. Page 1 line 20 through page 2 line 6. A person of ordinary skill in the art would have had a reasonable expectation of success utilizing and detecting IgE, because Wiegand et al. shown DNA ligands that were operable in this process with high affinity and accuracy. Page 38, lines 3-12.

With respect to the antibody binding characteristics recited in claims 26-28 these limitations are view as inherent properties, which are found in all antibodies. Absent evidence to the contrary they are viewed as obvious limitations found in antibodies.

A claim is anticipated if each element of the claim is found, either expressly described or under principles of inherency, in a single prior art reference, or that the claimed invention was previously known or embodied in a single prior art device or practice.

It has been held that the recitation that an element is "capable of" performing a function is not a positive limitation but only requires the ability to so perform. It does not constitute a limitation in any patentable sense. *In re Hutchison*, 69 USPQ 138.

III. Claims 19, 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Griffin et al. (US Patent #5,756,291) in view of Schultz et al. (US Patent #6,180,415) in further view of Sampson et al. (US Patent #6,054,274).

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It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize denaturing procedures and/or column separation procedures such as hybridization/polymerization as taught by Sampson et al. in the method of Griffin et al. (US Patent #5,756,291) in view of Schultz et al. (US Patent #6,180,415) Griffin et al. taught that the inventive method allowed for multiple hybridization and polymerization to produce enhanced detection of a target nucleic acid sequence. Column 3, lines 24-50.

A person of ordinary skill in the art would have had a reasonable expectation of success utilizing such materials, because they were already shown to be operable in the prior art.

One having ordinary skill in the art would have been motivated to do this because of the increased flexibility in detecting and analyzing the target molecule.

12. For reasons aforementioned, no claims are allowed.

Remarks

13. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

Nazarenko et al. (US Paten #5,866,336) disclose methods involving oligonucleotides with molecular energy transfer labels.

14. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 308-4242, which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (703) 305-0808. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

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